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Structure and function of milk allergens.

Wal JM.

Laboratoire Associe INRA-CEA d'Immuno-Allergie Alimentaire, DRM-SPI
Bat. 136 CEA de Saclay, 91191 Gif sur Yvette, France.

Proteins (CMP) involved in milk allergy are numerous and heterogeneous, with very few structural or functional common features. This heterogeneity is complicated by their genetic polymorphism, resulting in several variants for each protein. These variants are characterized by point substitutions of amino acids or by deletions of peptide fragments of varying size or by post-translational modifications such as phosphorylation or glycosylation. All of these modifications may affect allergenicity. No common molecular structure can be associated with allergenicity, although some homologous regions such as casein phospho-peptides can explain an IgE cross-reactivity. Three-dimensional structure is an important feature in CMP allergenicity but denatured and linear epitopes are also involved. Epitopes are numerous and widely spread along the CMP molecule. They may be located in hydrophobic parts of the molecule where they are inaccessible for IgE antibodies in the native conformation of the protein but become bioavailable after digestive processes. Peptides as short as ca. 12-14 amino acid residues may account for a significant part of the allergenicity of the whole molecule, which justifies the need to be careful before proposing any CMP hydrolysate for highly allergenic children.

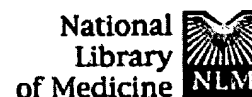
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Isoforms of atopic allergens with reduced allergenicity but conserved T cell antigenicity: possible use for specific immunotherapy.

Ferreira F, Hirthenlehner K, Briza P, Breiteneder H, Scheiner O, Kraft D, Breitenbach M, Ebner C.

Institute of Genetics and General Biology, University of Salzburg, Austria.

BACKGROUND: We analyzed the T cell activation potency and the IgE-binding properties (allergenicity) of nine isoforms of Bet v 1, the major allergen of birch pollen. **METHODS:** The capacity of recombinant Bet v 1 isoforms to bind serum IgE from allergic patients was evaluated by immunoblot experiments and skin prick tests. The potency of Bet v 1 isoallergens to activate T lymphocytes from birch-pollen-allergic patients was assayed using allergen-specific T cell clones. **RESULTS:** According to their ability to bind IgE from allergic patients in immunoblot experiments, Bet v 1 isoforms can be grouped into high-IgE-binding molecules and molecules with low/no IgE-binding activity. Representatively, isoform d was used in skin tests. Skin prick tests revealed no potency of this isoform to induce wheal and flare reactions in the skin of birch-pollen-allergic individuals. In contrast, isoform a and natural Bet v 1 displayed high allergenicity in vivo. On the other hand, Bet v 1 isoform d (low allergenicity) displayed significant higher T cell activation potency when compared to isoform a (high allergenicity). **CONCLUSION:** Based on these findings, we propose a new form of specific immunotherapy using hypoallergenic recombinant allergen isoforms.

PMID: 9130500 [PubMed - indexed for MEDLINE]

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1: J Allergy Clin Immunol. 1997 Jun;99(6 Pt 1):781-7.

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J Allergy Clin Immunol

Mapping of IgE-binding epitopes on the recombinant major group I allergen of velvet grass pollen, rHol 1 1.

Schramm G, Bufe A, Petersen A, Haas H, Schlaak M, Becker WM.

Forschungszentrum Borstel, Germany.

BACKGROUND: New and more successful approaches to diagnosis and therapy of allergic diseases require a more subtle understanding of the structure and the epitopes on the allergen molecule. **OBJECTIVE:** This study was done to obtain more information on the structure and the IgE-binding epitopes of a major allergen of velvet grass pollen, Hol 1 1. **METHODS:** We cloned Hol 1 1 from a complementary DNA library and performed B-cell epitope mapping with 21 recombinant fragments expressed as fusion proteins in *Escherichia coli*. The fragments were analyzed by Western blotting with sera from 50 different patients. **RESULTS:** The patients' sera individually recognized at least four different IgE-binding regions (amino acids 1 to 27, 61 to 76, 84 to 105, and 158 to 240). According to their binding patterns with these epitopes, they were divided into five groups. Most sera (92%) bound to the C-terminal peptide (158 to 240), which consists of more than 80 amino acids, whereas there was virtually no binding to smaller fragments covering this region. In contrast to the C-terminal peptide, the IgE-binding peptides on the N terminus and on the middle region of the molecule were of a smaller size (15 to 30 amino acids). **CONCLUSIONS:** The major group I allergen of velvet grass bears at least four different IgE-binding epitopes, which were individually recognized by sera from different patients. The C terminus represents the major IgE-binding region and contains at least one discontinuous IgE-binding epitope, whereas the N terminus and middle region of Hol 1 1 seem to contain continuous IgE-binding epitopes.

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